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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,365	03/09/2001	Martha Jo Whitehouse	PP01671.003	8316

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary	Application No. 09/802,365	Applicant(s) Whitehouse
	Examiner Fozia Hamud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 18, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 4-17, and 19-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-17, and 19-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Office Action

1. Receipt of Applicants' arguments and amendments filed in Paper No.10 on 18 February 2003 is acknowledged. Claim 3 and 18 have been canceled and claim 1, 4, 16, 19 and 21 have been amended. Thus claims 1-2, 4-17 and 19-29 are pending and under consideration.

2. The following previous objections and rejections are withdrawn in light of Applicants amendment filed in Paper No.13, 02/18/03:

(I) The objection to the specification for containing an embedded hyperlink.

(II) The objection to the specification for not containing an abstract.

(III) The objection to claims 1, 6, 16 for reciting non-elected species.

Response to Arguments:

Claim Rejections-35 USC § 112

3a. Claims 1-2, 4-17 and 19-29 stand rejected under 35 U.S.C. §112, first paragraph for reasons of record set forth in Paper No:9 mailed on 18 November 2002, section 4a, pages 3-5.

Applicants' first argument is that there is no requirement of 35 U.S.C §112, first paragraph enablement that any particular sort of data, such as experimental data be provided. Instead the requirement for adequate enablement is simply one of experimentation that is not undue. Applicants' second argument is that the claimed invention is based on anecdotal observation during a phase I clinical trial investigating the use of FGF-2 to treat coronary artery disease, in which patients receiving doses of FGF-2 treatment in the range provided in the instant specification, volunteered that their sexual activities were more satisfactory as a result of improved erectile function.

Applicants conclude that the efficacy of the presently claimed invention has already been demonstrated. Applicants' third argument is that one of skill in the art can readily practice the claimed invention and can further assess the efficacy of the claimed method, without undue experimentation by administering FGF at the recommended dosage, in accordance with the recommended route of administration and assess the desired therapeutic response, by measuring the ability of the patient to achieve and sustain an erection.

Applicants' arguments have been fully considered, but are not deemed persuasive. With respect to Applicants' first argument, although working examples are not required under 35 U.S.C §112, first paragraph, they are one of the factors that must be considered when determining enablement, especially in light of the lack of guidance in the specification and the nature of the invention, since penile erection involves a complex interaction between the CNS and local factors that are modulated by psychological and hormonal factors. And since Applicants provide no sound scientific reasoning as to why FGF-2 should have an effect on erectile dysfunction. Instant specification is based solely on a hypothesis, however, Applicants provide no evidence to support this hypothesis. Applicants' second argument is not found persuasive, because, there is no disclosure of the observations made during the phase I clinical trial that Applicants are referring to in the instant specification. If Applicants wish that the evidence disclosed in the phase I clinical trial to be considered, they must file a Declaration so that it can be part of the record. With respect to Applicants' third argument, it would be undue experimentation to test the effect of FGF-2 or muteins or biologically active fragments of FGF-2, on erectile dysfunction and also to test their effects on the many disease conditions that are associated with erectile dysfunction, such as heart disease,

peripheral vascular disease, diabetes mellitus, thus the agent to be used for erectile dysfunction must also not have any detrimental effects on the patient. It would also be undue experimentation to conduct appropriate experiments and use appropriate controls to test the effectiveness of FGF-2 or muteins in treating or preventing erectile dysfunction. Instant specification only provides a hypothesis that angiogenic agents or growth factors encourage endothelial cell proliferation, to restore endothelial cell function and to promote angiogenesis, particularly to promote blood flow, however, this is not adequate guidance as to the effectiveness of FGF-2 or mutiens to treat or prevent erectile dysfunction, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Therefore, the claimed invention is not enabled based on the teachings of the instant disclosure alone.

3b. Claims 6-14 and 21-29 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No:9 mailed on 18 November 2002, section 4a, pages 5-6.

Applicants argue that the definition of an angiogenitically or biologically active fragment of FGF-2 (applying to both SEQ ID NO:2 and 4), is the fragment that has about 80% of the 146 residues of SEQ ID NO:2 and retains the angiogenic or biological effect of the FGF- of SEQ ID NO:2 or 4 and that angiogenitically active muteins of FGF-2 are disclosed in U.S. Patent 5,859,208 and 5,852,177. Applicants further argue that the biologically active muteins typically encompass those terminally truncated fragments of an FGF-2 that have at least residues that correspond to 30-

110 of rFGF-2 or 18-146 of SEQ ID NO:2. Thus, Applicants conclude that the specification provides guidance as to which areas of FGF-2 are important for cellular and heparin binding, and general guidance as to conservative substitutions to be made to FGF muteins.

These arguments are not found persuasive, because with the exception of SEQ ID NO: NO: 2 or 4, the skilled artisan cannot envision the detailed structure of the encompassed fragment or mutein that has about 80% of the 146 residues of SEQ ID NO:2 or 4, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. With respect to angiogenitically active muteins of FGF-2, Applicants should recite the specific FGF-2 muteins that are disclosed in U.S. Patent 5,859,208 and 5,852,177, which Applicants consider have the ability to treat or prevent erectile dysfunction. Applicants argue that biologically active muteins typically encompass those terminally truncated fragments of an FGF-2 that comprise residues 30-110 of rFGF-2 or 18-146 of SEQ ID NO:2, however, these specific structural limitations are not recited in the claims.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE?MONTH shortened statutory period, then the shortened statutory period will expire on the

date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
22 April 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600